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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/737,403	12/16/2003	Richard Coale Willson III	015AUS	6655

26830 7590 09/19/2007

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EXAMINER	
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ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
09/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/737,403	WILLSON ET AL.	
	Examiner	Art Unit	
	Samuel Woolwine	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Note

As per telephonic confirmation with Richard Willson Jr on 9/10/2007, claims 1-24 are pending.

Election/Restrictions

Applicant's election of the species (1) single stranded regions, (2) chromatography, and (3) denaturation in the reply filed on 8/11/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's cancellation of claim 25 in the response filed 8/11/2007 is noted.

Claim Objections

Claim 9 is objected to because of the following informalities: there is an unpaired ")" after the word "contaminant". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6, 8-10, 12 and 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4 and 19-22 recite the limitation "the product" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claims or in claim 1,

from which these claims depend. It cannot be determined what "the product" refers to: the affinity handle? the nucleic acid being separated? or does it refer to some product from which the nucleic acid is to be separated? The examiner will assume either of the latter two options. If these interpretations are the intent, Applicant is advised to amend claim 1 to recite a product, "wherein the product is either a nucleic acid to be purified, or a product (which can be either a nucleic acid or a non-nucleic acid product) from which undesired nucleic acid is to be separated".

Claims 3 and 4 are also rejected under this section because it cannot be understood what the word "selective" in the phrase "a moiety that is sensitive to host genomic DNA contamination selective such as..." means. For purposes of further examination, the examiner will construe this term to mean "during selective separation", based on the language of claim 1.

As claims 5 and 6 depend from claim 4, they are rejected under this section for the reasons discussed above.

Also regarding claims 3, 8, 9 and 10, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Since claim 12 depends from claim 9, it is rejected for the same reason. For purposes of further examination, the examiner will construe the limitations following the phrase "such as" to be optional.

Also regarding claims 8 and 9, the phrases "after another thermally based process" and "after another alkali based process" in claims 8 and 9, respectively, suffer from a lack of antecedent basis, because there is no initial thermally based process or

alkali based process recited in these claims or in claim 1, from which these claims depend. Applicant may wish to either amend claim 1 to recite such initial processes, or simply amend claims 8 and 9 to recite, respectively, "after a thermally based process..." and "after an alkali based process...". For purposes of further examination, the claims will be construed based on the latter suggestion.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6-8, 10, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Verdine et al (WO 98/00435).

With regard to claims 1, 2 and 7, Verdine teaches a method comprising introduction of a single-stranded region of nucleic acid as an affinity handle into the desired nucleic acid, followed by capture of the desired nucleic acid by a technique that is selective for the characteristics of the affinity handle (see page 10, lines 1-5; page 11, line 1 through page 12, line 4). Verdine introduced a single-stranded region of nucleic acid into a desired nucleic acid by way of using the single-stranded region of nucleic acid as a primer to PCR amplify a target nucleic acid. One of the primers was tagged with six successive 6-histaminylpurine residues (see page 9, lines 20-22 and page 10, line 3, "H_6-tagged primer"). Verdine denatured the resulting PCR product in 6M

guanidinium-HCl (page 11, lines 6-7), thus exposing the single-stranded affinity handle. The tagged strand of the PCR product was immobilized on Ni^{2+}-NTA resin (page 11, lines 6-7), allowing it to be separated from the other strand. Note that either the tagged on non-tagged strand of the PCR product may be considered the "desired" product.

With regard to claims 3 and 4, note that the desired (or undesired) product (i.e. the tagged or non-tagged strand of the PCR product) comprises single-strandedness (i.e. it *is* a single stranded molecule).

With regard to claim 6, Verdine teaches IMAC (see page 11, lines 1-7).

With regard to claim 8, Verdine produced a product by PCR (page 10, lines 1-5). PCR comprises thermal denaturation.

With regard to claim 10, Verdine teaches PCR (page 10, lines 1-5), which comprises selective thermal denaturation and renaturation. This also meets the claim based on the species of "the use of primers".

With regard to claim 14, Verdine teaches adsorption on chelated metal (page 11, lines 6-7).

With regard to claim 16, Verdine teaches a column (page 9, lines 5-6). It is noted that the claim term "spin" does not distinguish over Verdine, since any column could be spun. The claim as written only requires the "use" of spin columns; it does not require the columns to be spun.

Claims 1, 2, 5, 7, 8 and 19 rejected under 35 U.S.C. 102(b) as being anticipated by Heisler et al (US 5,843,654).

Heisler teaches a method for the construction of recombinant Taq polymerases (see Example 2, beginning in column 59, especially lines 40-45). Heisler teaches cloning the recombinant genes into a plasmid that introduces a "His-Tag" (see column 62, lines 64-66 and column 63, lines 12-20). Heisler teaches purification of the recombinant proteins on Ni^{++} column (column 63, lines 50-53). Heisler teaches that the production of the cell lysates comprising the recombinant Taq polymerases includes heat lysis (column 64, lines 48-52), followed by a second heating step (column 64, lines 63-64).

With regard to claims 1, 2 and 7, Heisler teaches the introduction of a structural affinity handle ("His-Tag", which may be regarded as single-strandedness, since the handle comprises a single strand of six histidine residues) to the desired moiety (the recombinant Taq), followed by capture of the desired or undesired nucleic acids by techniques which are selective for the characteristics of the affinity handle (purification on the Ni^{++} column). Although this may seem confusing, a careful analysis of the claim shows that all that is required is that desired or undesired nucleic acids are captured by techniques that are selective for the characteristics of the affinity handle. The claim does not require that an affinity handle be introduced into nucleic acids (although this is one option recited by the claim). The claim requires introduction (or enhancement or stabilization) of an affinity handle into desired or undesired nucleic acids *or* moieties. The claim does, however, require that desired or undesired nucleic acids be captured.

This limitation is inherently met by the method taught by Heisler. Heisler teaches thermal lysis of host cells (column 64, lines 48-52), which would release the nucleic acid

content of the cells. Heisler teaches a secondary heating step at 75°C for 1 hour, whereas Applicant's example 5 in the specification (which also involves purification of recombinant Taq) heats for 80°C, but for 1 minute. If heating at 80°C for 1 minute is sufficient to alter the contaminating genomic DNA to allow it to interact with the chelated metal of the affinity column, then certainly a mere reduction of 5°C would be more than compensated for by the 60-fold increase in incubation time. In addition, the lysate would comprise some nucleic acids that were single-stranded even without the heating step (such as mRNA, tRNA and rRNA). Since Applicant's assert in their disclosure that it is the "exposure" of bases that results in the adsorption to chelated metals during IMAC (immobilized-metal affinity chromatography), then such would also have occurred when Heisler passed his cells lysates over the Ni^{++} columns.

With regard to claim 5, Heisler teaches the manufacture of recombinant Taq polymerase (see Example 2, beginning in column 59, especially lines 40-45).

With regard to claim 8, Heisler teaches that the production of the cell lysates comprising the recombinant Taq polymerases includes heat lysis (column 64, lines 48-52), followed by a second heating step (column 64, lines 63-64).

With regard to claim 19, Taq is a protein.

Claims 1-4, 7, 9-12, 16, and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Pham et al (BioTechniques, 20(3):492-497 (1996)).

With regard to claims 1, 2, 7 and 9, Pham introduces single-stranded "affinity handles" into undesired nucleic acids by alkaline lysis (see figure 1), rapidly neutralized

(page 493, column 1, first paragraph), followed by capture of the undesired nucleic acids (denatured single-stranded DNA and RNA) on SSAM matrix, which is selective for the characteristics of the single-stranded "affinity handles" (see page 492, column 2, first full paragraph and see page 493, column 1, first paragraph).

With regard to claims 3 and 4, Pham's product (plasmid) is double-stranded, whereas the undesired nucleic acids are single-stranded. Pham's product would be "sensitive" to contaminating genomic DNA.

With regard to claim 10, alkaline lysis (see figure 1) would produce alkaline denaturation.

With regard to claims 11 and 12, Pham refers to his product as "purified supercoiled DNA" (page 494, column 2). Furthermore, Pham electrophoresed samples of his product (see figure 2), which would inherently "remove" linear and open circular forms from the supercoiled form.

With regard to claim 16, Pham's method involves the use of spin columns (see title and page 493, column 1, first paragraph "CHROMA SPIN+TE-400 Column").

With regard to claims 20, 21 and 22, while Pham was attempting to purify plasmid (and thus, in Pham's view, the "product" would be a plasmid, meeting the limitations of claim 20), it is noted that the method also achieves a purification of RNA and genomic DNA, which bind to the SSAM matrix. Therefore, said RNA and genomic DNA may also be regarded as "products". The claim term "desired" does not distinguish over the method of Pham, because what is "desired" is nothing more than a mental state of the one who practices the method.

Claims 1-4, 6, 7, 10, 14-17, 23 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Willson et al (US 2004/0152076) or alternatively under 35 U.S.C. 102(a) as being anticipated by Murphy et al (WO 02/46398). As the disclosures of these references are identical, reference will only be made to teachings in US 2004/0152076.

With regard to claims 1, 2 and 7, Willson teaches an embodiment in which a deoxyribose tail is used as a tag to bind a PNA (peptide nucleic acid) to an IMAC column (paragraph [120]). This represents the introduction of a single-stranded region of nucleic acid as an affinity handle.

With regard to claims 3 and 4, note that the desired product (i.e. the peptide nucleic acid) comprises single-strandedness (i.e. it *is* a single stranded molecule).

With regard to claim 6, Willson teaches IMAC (paragraph [0120]).

With regard to claim 10, Willson teaches the "use of primers or other nucleic acid fragments" (the deoxyribose tail is an "other nucleic acid fragment"; paragraph [0120]).

With regard to claim 14, Willson teaches IMAC (paragraph [0120]), which comprises adsorption on chelated metal (paragraph [0007]).

With regard to claims 15, 16, 17, Willson teaches multi-channel plates ("well plate"), spin columns and magnetic particles (page 5, Table A, Parameter: Support Shape).

With regard to claim 23, Willson teaches RPC (reverse phase chromatography; "Reverse Phase Resin", which implicitly teaches reverse phase chromatography; page 6, Table A, line 2 under heading "Preferred").

With regard to claim 24, Willson teaches HIC (hydrophobic interaction chromatography; page 5, Table A, last 3 lines under heading "Preferred").

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Willson et al (US 2004/0152076) or Murphy et al (WO 02/46398) in view of Hawkins (US 5,898,071).

The teachings of Wilson and Murphy have been discussed. Neither of these references teaches processing multiple samples in parallel.

Hawkins teaches methods of nucleic acid purification and teaches that an "advantage of using a microtitre plate is that many samples can be isolated in parallel" (column 10, lines 54-60).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention of the instant application was made to modify the method of either Willson or Murphy to process multiple samples in parallel, because Hawkins teaches this to be advantageous.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

scw

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